THE AMERICAN JOURNAL OF PHARMACY

PUBLISHED BY AUTHORITY OF THE

PHILADELPHIA COLLEGE OF PHARMACY

EDITED BY

HENRY KRAEMER

PUBLICATION COMMITTEE FOR 1914

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VOLUME 86

PHILADELPHIA
1914

THE AMERICAN
JOURNAL OF PHARMACY

JANUARY, 1914

THE ASSAY OF MERCURIC CHLORID TABLETS.

By Robert M. Chapin,
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At the present time mercuric chlorid tablets, especially those prepared after the well-known Wilson formula, are very widely used, and are used moreover with implicit confidence in the accuracy of their declared content of mercuric chlorid under circumstances which render such accuracy a matter of considerable importance to individual welfare and to the public health in general. There can be no question of the desirability of assay methods which shall be fairly accurate, yet simple and rapid enough to be freely used by manufacturers, pharmacists, hospitals, and sanitary officials at a minimum of expense and chemical equipment.

Several years ago Rupp [1] proposed a rapid method for the determination of mercury in various compounds, involving the following steps: (1) Reduction to metallic mercury by formaldehyde in alkaline solution in presence of potassium iodid; (2) solution of the precipitated mercury in excess of standard iodin solution after acidification with acetic acid; and (3) titration of excess iodin by standard sodium thiosulphate. A modification of the method is now official in the German Pharmacopœia for the assay of tablets composed of mercuric and sodium chlorids.

In this country Smith [2] has thoroughly studied the Rupp method when applied to pure mercuric chlorid, obtaining, when certain modi-

[1] Rupp, E. Ueber die volumetrische Bestimmung des Quecksilbers. *Berichte der Deutschen Chemischen Gesellschaft*, Vol. 39, No. 14, pp. 3702–3704. Berlin, Nov. 10, 1906.

[2] Smith, Carl E. Volumetric determination of mercury. American Journal of Pharmacy, Vol. 83, No. 7, pp. 311–315. Phila., July, 1911.

fications were introduced, a recovery of 99.8 to 100.3 per cent. of the mercuric chlorid employed. Smith's modifications involved (1) the use of a larger amount of substance and reagents to reduce experimental errors, (2) a longer time of action by formaldehyde to insure complete reduction to metallic mercury, and (3) a much less degree of acidification before addition of iodin, since large amounts of free acetic acid tend to produce low results. Smith states that similarly good quantitative results were obtained when the method was applied to mixtures of mercuric chlorid and ammonium chlorid colored with aniline dyes. That is, the modified method is implied to be applicable to commercial tablets prepared after Wilson's formula (mercuric chlorid, 7.3 grains; ammonium chlorid, 7.7 grains; coloring matter, q.s.).

In this laboratory Smith's statements and results were confirmed on solutions of pure mercuric chlorid. Utter failure, however, followed attempts to apply his method either to commercial tablets or to similar laboratory mixtures of mercuric and ammonium chlorids. Abnormal precipitates appeared after addition of iodin, and results obtained were erratic and much too low. At the same time the method given in the German Pharmacopœia, slightly modified, was found to work smoothly and quantitatively.

The addition of formaldehyde to a solution of ammonium salts produces hexamethylenamin, which is known to form difficultly soluble compounds with both iodin and mercuric salts.[3] In Smith's modification, then, conditions appear to be such as to permit the formation and separation of hexamethylenamin compounds to the resultant vitiation of the process, while in the method of the German Pharmacopœia the greater dilution at which the process is worked either inhibits the formation of such interfering substances, or, more probably, is sufficient to retain them in solution and hence in a harmless condition. At all events, if, in addition to other minor modifications later to be noted, a volume of 75 c.c. of water is added at the time the contents of the flask are acidified before the addition of iodin, no abnormalities appear in the working of Smith's process, and the results are equally accurate in the presence or absence of ammonium chlorid.

Inasmuch as the method finally chosen here as most satisfactory is

[3] Cohn, G. Die Verbindung des Urotropins. *Pharmazeutische Zentralhalle*, Vol. 52, No. 44, pp. 1173–1179. Dresden, Nov. 2, 1911.

somewhat different in details from either of the two modifications already noted, the points of difference and the reasons therefor will be discussed.

In the first place, while it is true that the use of large amounts of substance and reagents tends to reduce the relative magnitude of experimental errors, there is a point beyond which any slight possible gain in accuracy is attained only at the sacrifice of an unwarranted measure of simplicity, convenience, and rapidity. It is certainly open to question whether this point is not passed by Smith's modification with its considerable consumption of standardized solutions, especially when the total volume of liquid worked with is increased by the 75 c.c. of water here found necessary to prevent interference by hexamethylenamin compounds. The writer therefore recommends the employment of 0.20 to 0.25 gram of mercuric chlorid for each test, and the addition of 25 c.c. of tenth-normal iodin.

Experiment 1.—To test the limits within which the results of parallel determinations may fall if the above proportions are used, a series of seven parallel tests were made on a solution of commercial tablets, using the equivalent of one-half tablet for each test. Aside from the use of volumetric apparatus which had passed the requirements of the Bureau of Standards, no precautions not employed in ordinary quantitative work in any laboratory were observed. The cubic centimetres of iodin solution (tenth-normal × 0.978) consumed in the solution of mercury were as follows: (1) 17.72; (2) 17.73; (3) 17.68; (4) 17.69; (5) 17.72; (6) 17.73; (7) 17.65; an extreme difference of 0.08 c.c. The average weight of mercuric chlorid per tablet was therefore found to be from 0.4677 to 0.4698, a difference of 0.45 per cent. The range of variation reported by Smith in a series of five tests by his method on pure mercuric chlorid was 0.5 per cent.

Secondly, the proportion of potassium iodid should be considerably increased over that employed by either Rupp or Smith in order to avoid the formation of mercurammonium compounds which result when caustic alkali in excess is added to a solution containing potassium mercuric iodid and ammonium salts, as in the well-known "Nessler test."

Thirdly, the presence of ammonium salts in one way or another operates to retard the reduction to metallic mercury so that it is not complete in 5 minutes though apparently so after 10 minutes.

Lastly, commercial formaldehyde solutions often contain foreign substances, some of which conceivably may consume iodin, and in fact such solutions have here been found which did possess this

power in slight but distinct degree. Hence a standard thiosulphate solution should be made the basal standard against which the iodin solution is standardized by running a blank assay with the other solutions and reagents intended for actual use.

The method finally chosen for tablets after Wilson's formula is as follows: Weigh 5 tablets, dissolve in water, dilute to 100 c.c., and pass through a dry filter, discarding the first 20 c.c. of filtrate. From the remainder pipette 10 c.c. (equivalent to one-half tablet) into a glass-stoppered 250 c.c. Erlenmeyer flask, add 2½ grams pure powdered potassium iodid, mix to entirely dissolve, and then wash down the sides of the flask with 20 c.c. of normal caustic alkali. Add exactly 3 c.c. of 37 per cent. formaldehyde solution, mix thoroughly, and let stand for at least ten minutes, swirling the flask occasionally. Then wash down the sides of the flask with a mixture of 5 c.c. of 36 per cent. acetic acid with 25 c.c. water; mix, and without delay run in from a burette 25 c.c. of tenth-normal iodin while constantly swirling the flask. Stopper the flask tightly, shake vigorously for three minutes, then after giving the contents a final swirling motion leave at rest for two minutes. If then no undissolved mercury can be detected at the bottom the stopper is removed, rinsed, together with the neck of the flask, with a stream from a wash-bottle, and the excess iodin titrated with tenth-normal sodium thiosulphate, adding starch solution only when the iodin is nearly consumed.

Standardize the iodin solution by running a blank assay on 10 c.c. distilled water.

Subtract the volume of thiosulphate solution used in the assay from that used in the blank. The difference multiplied by the factor 0.0271 for strictly tenth-normal sodium thiosulphate will give the average weight of mercuric chlorid per tablet. For a direct check upon the value of the sodium thiosulphate solution run an assay on 10 c.c. of a 2½ per cent. solution of mercuric chlorid of known purity.

While mercuric chlorid is the important active ingredient of tablets made according to Wilson's formula, nevertheless ammonium chlorid is an essential part of the formula, added in order to render the tablets easily soluble and to inhibit the formation of insoluble, and hence inactive, compounds of mercury. An assay of such tablets

ought therefor to include an estimation of ammonium chlorid, especially when a simple and convenient method is available.

The method for ammonium chlorid here adopted is an adaptation of the process of Ronchèse,[4] which is based on the reaction between formaldehyde and a neutral ammonium salt, whereby methylenamin, $(CH_2)_6N_4$, is formed, the acid originally contained in the ammonium salt being released and becoming titratable with standard caustic alkali and phenolphthalein. The strengths of reagents, etc., recommended by Wilkie [5] have been adopted.

Titration by standard alkali and phenolphthalein can not of course be conducted in presence of mercuric chlorid. This difficulty, however, is easily overcome by throwing the mercury into a complex ion through the addition of potassium iodid. The method is as follows: Into each of two 150 c.c. Erlenmeyer flasks pipette 5 c.c. (one-fourth tablet) of the tablet solution previously prepared for the estimation of mercuric chlorid (5 tablets per 100 c.c.) and add to each flask 2 c.c. of a 20 per cent. solution of potassium iodid.

Dilute one volume of 37 per cent. formaldehyde solution with three volumes of water, measure 20 c.c. of the mixture into a small flask, add 0.5 c.c. of phenolphthalein indicator solution, neutralize with tenth-normal barium hydrate or caustic alkali, then flow the solution over the sides of one of the flasks (flask A) containing tablet solution, and mix well. To the other flask (flask B) containing tablet solution add about 65 c.c. water.

Now add to flask A 25 c.c. water and titrate with tenth-normal barium hydrate or tenth-normal caustic alkali free from carbon dioxid until, by using flask B as a standard for comparison, a color change is perceptible (titration A).

Add methyl red to flask B and titrate with either tenth-normal acid or alkali as needed (titration B).

To titration A add titration B if performed with acid, or subtract if performed with alkali. The resultant figure multiplied by the factor 0.0214 for strictly tenth-normal alkali will give the average weight of ammonium chlorid per tablet.

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[4] Ronchèse, A. Nouveau procédé de dosage de l'ammoniaque. *Journ. de Pharmacie et de Chimie*, Vol. 25, No. 12, pp. 611–617. Paris, June 16, 1907.

[5] Wilkie, John M. The Ronchèse method of determining ammonia and its extension to the determination of the total acid content of organic ammonium salts and ammoniacal solutions. *Journal of the Society of Chemical Industry*, Vol. 29, No. 1, pp. 6–7. London, Jan. 15, 1910.

For a direct check upon the value of the tenth-normal alkali run an assay upon 5 c.c. of a 2½ per cent. solution of pure ammonium chlorid.

Solutions, reagents, and water used should be free from carbon dioxid.

Ordinarily titration B is very small, sometimes zero, but usually calling for the addition of a few drops of tenth-normal acid.

As respects the end points with the indicators it is only possible to state that up to the present time no blue or green tablets which have been received by the writer have presented the slightest difficulty. The characteristic colors of the indicators of course do not appear in the presence of other coloring matter, but the change of tint, if standards of comparison are used, is delicate and distinct. No red tablets have been received for examination.

The reliability of the method may be shown by noting a few results.

Experiment 2.—Four tests made on 5 c.c. of a solution of 2 grams each of commercial C.P. chlorids of mercury and ammonium per 100 c.c. gave the following figures for titration A (titration B = O), made with barium hydrate solution (tenth-normal × 1.021) which had been standardized against a laboratory stock solution of half-normal hydrochloric acid: (1) 18.24 c.c.; (2) 18.26 c.c.; (3) 18.29 c.c.; (4) 18.26 c.c.; an extreme difference of 0.05 c.c. and a recovery of 99.6 to 99.9 per cent. of the ammonium chlorid employed.

Experiment 3.—Three titrations made on 5 c.c. of the solution of commercial tablets employed in Experiment 1 gave titration B as zero, and titration A as (1) 22.64 c.c.; (2) 22.58 c.c.; (3) 22.62 c.c.; an extreme difference of 0.06 c.c.

It appears, therefore, that assay methods are now available for accurately and conveniently estimating mercuric and ammonium chlorid in commercial tablets. Knowing the weight of tablets taken to prepare the stock solution for assay, estimation of coloring matter and "filler" is merely a matter of subtraction. Further possible tests, such as degree of solubility, amount of insoluble matter, and uniformity of weight of individual tablets, are a matter of discretion with the analyst and need no discussion.

SEASONAL VARIATIONS IN THE RESISTANCE OF GUINEA PIGS TO POISONING BY OUABAIN AND BY LIQUID PREPARATIONS OF DIGITALIS.

By C. C. Haskell, A.B., M.D.

In a previous paper [1] it has been shown that guinea pigs are more resistant to poisoning by ouabain during certain months of the year than at others. These results were confirmed in a general way by Vanderkleed and Pittenger [2] in a subsequent publication. It is of interest to compare the results secured in this laboratory with those reported by Vanderkleed and Pittenger.

I have used male pigs exclusively, and have been compelled to employ animals differing largely in weight; the majority, however, weighed 250 grams or more, so it seems best to compare my results with those obtained by Vanderkleed and Pittenger using "large males." In order to facilitate comparison, the average minimum lethal dose has been expressed in fractions of a gram per gram body weight and put in the following tabular form:

Table I.

Month.	Vanderkleed and Pittenger.	Haskell.
January.....1912	.00000025	.00000052+
February.....1912	.00000030	.00000037
March.....1912	.00000032	.00000036
April.....1912	.00000033	.00000040
May.....1912	.00000033	.00000045
June.....1912	.00000033	.00000040
July.....1911	.00000021	.....
August.....1911	.00000021	.00000029
September.....1911	.00000021	.00000030
October.....1911	.00000021	.00000036
November.....1911	.00000024	.00000052
December.....1911	.00000028	.00000052

It is readily seen that the same general conclusion is deducible from both series of tests: the resistance of the pigs is least during the hot summer months and greatest in the cooler weather. In August, there is a difference of 38 per cent. between the lethal dose required

[1] Am. Jour. Pharm., Vol. 84, No. 6, p. 241, 1912.
[2] *Jour. Am. Ph. Assoc.*, Vol 11, No. 5, p. 558, 1913.

in Indianapolis and that determined in Philadelphia; and in January, the enormous preponderance of 108 per cent. is shown by the Indianapolis lethal dose. Obviously, it is scarcely to be expected that we should secure very closely comparable results in assaying a galenical if such divergence occurs in testing a "pure principle."

In endeavoring to account for this disagreement, the technic employed should be closely scrutinized. It is a well-recognized fact that testing digitalis upon frogs requires the closest attention to details and necessitates the avoidance of any disturbing factors such as large variations in the weight of the animals and, especially, extremes of temperature. From previous statements of those who have employed the guinea pig method, one is led to infer that such extreme caution is not necessary when this method is used, and the results of Vanderkleed and Pittenger seem to show that weight and age are factors of little moment.

In all of my experiments, a solution of ouabain, 1 to 10,000 in 25 per cent. alcohol, was used. Vanderkleed and Pittenger do not state whether alcohol was present in the solutions they employed, but its absence would explain the smaller dose determined by them as compared to the dose I found necessary in August, because alcohol exerts a similar antagonistic action toward the absorption of subcutaneously-administered ouabain as it does toward digitalis administered in this way. Some other explanation, however, is necessary to account for the difference between the minimum lethal dose determined in Indianapolis in January (.00000052 +) and that determined in Philadelphia for the same month (.00000025). The pigs used by Vanderkleed and Pittenger were kept in fairly warm quarters; while our animals were subjected to considerable variations in temperature, the thermometer occasionally registering as low as 50° F. This, I believe, has an important bearing on the resistance of the guinea pigs and, together with the influence of the alcohol used in my experiments, may serve to explain the difference in the lethal dose as determined in the winter months.

Since this earlier report, the minimum lethal dose of ouabain in 25 per cent. alcohol has been determined upon guinea pigs in a number of different months and a comparison is of some interest. In Table II such a comparison is given.

These figures indicate that the temperature influences the powers of resistance. During the extremely cold winter of 1911–12 the

dose for November, December, and January was .00000052: while during the much milder winter of 1912–13, the lethal dose was smaller. Where comparison is possible in other months, the difference never amounts to more than 15 per cent.

TABLE II.

Month.	1911.	1912.	1913.
January	.....	.00000052+	.00000040
February	.....	.00000037	.00000042
March	.....	.00000036	.....
April	.....	.00000040	.00000037
May	.....	.00000045	.00000045
June	.....	.00000040	.....
July	.....	.....	.00000025
August	.00000029	.....	.00000025
September	.00000030	.00000036	.....
October	.00000036	.00000042	.....
November	.00000052	.00000040	.....
December	.00000052	.00000045	.....

Seasonal variations in the resistance of test animals may be obviated by the use of a satisfactory standard, and Vanderkleed and Pittenger suggest the use of ouabain when galenicals of the "heart tonic" group are tested upon guinea pigs. The use of ouabain is justified, however, only when it has been shown that the variations in the resistance toward poisoning by ouabain parallels that toward poisoning by the galenicals under consideration. Opportunity has occurred to determine the minimum lethal dose of a small number of samples of tincture and fluid extract of digitalis at different seasons of the year. Some of the tinctures were made by the U.S.P. method and some were made with a menstruum containing 75 per cent. alcohol. All of the fluid extracts were made with a menstruum containing 70 per cent. or 80 per cent. alcohol.

In testing the tinctures, portions were evaporated to a semi-solid consistence upon the water-bath and the residue suspended in an amount of distilled water equal to the original volume of the portion taken for evaporation. The same procedure was followed with the fluid extracts, save that the volume of distilled water was five times that of the fluid extract taken. For reasons that will be apparent later; it is desirable that the preparations be divided into two groups; one comprising preparations containing about 50 per

cent. alcohol; the other comprising those containing from 70 to 80 per cent. alcohol.

The comparison of the lethal doses for two tinctures made with 50 per cent. alcohol and the lethal dose for ouabain during the same months is given in Table III.

TABLE III.

	June, 1912.	Oct., 1912.	Dec., 1912.	Jan., 1913.	Aug., 1913.
Ouabain.....	.0000004	.00000042	.00000045	.0000004	.00000025
Tr. Digitalis U. S. P. 434900.....	.004	.004	.007+	.0065	.0042
Tr. Digitalis U. S. P. 457579.....	.....	.....	.0075	.....	.0052

So far as can be judged by this limited number of experiments, "seasonal" variations in the resistance of guinea pigs toward poisoning by ouabain and by tinctures of digitalis made with 50 per cent. alcohol follow the same general curve. In January, 1913, the lethal dose for Tincture 434900 was .0065, while in July, 1913, it showed a decrease of 35.4 per cent.: the lethal dose of ouabain showed a decrease of 37.5 per cent. during the same time. In December, 1912, the dose of Tincture 457579 was .0075, while in July, 1913, it was 30.6 per cent. less: the dose of ouabain suffered a decrease of 44 per cent.

In testing the preparations containing relatively high percentages of alcohol, entirely different results were obtained. These are so surprising that it was only after confirming them repeatedly that I could feel that they were not due to some error in testing. The tests were carried out in a manner exactly similar to those dealing with the tinctures just discussed and the difference in the behavior seems to depend upon an essential difference in the composition of preparations made with 50 and 75 per cent. alcohol respectively.

From these results, it is evident that no seasonal variation has been observed in the resistance of guinea pigs to poisoning by fluid preparations of digitalis made by percolation of the leaf with menstrua containing 70 to 80 per cent. alcohol. Tinctures made with 75 per cent. alcohol differ in several important points from those made with 50 per cent. alcohol, but it seems almost incredible that the resistance of guinea pigs to poisoning by the two should follow

TABLE IV.

	Ouabain[1]	Tr. Digitalis 471124	Tr. Digitalis 461011	Tr. Digitalis 467056	Tr. Digitalis[2] 24678	F. E. Digitalis 461015	F. E. Digitalis 1654092
Jan. 1912	52						
1913	40	.....	.....	.0024*	.0025		
Feb. 1912	37						
1913	42						
Mar. 1912	36	.....	.....	.....	.0025		
1913	.....	.0027					
Apr. 1912	40	.....	.....	.....	.0030		
1913	37						
May 1912	45						
1913	45						
June 1912	40						
1913							
July 1912							
1913	25	.....	.....	.....	.0025	.00022	.00047
Aug. 1912	29						
1913	25	.0025	.0020	.0023			
Sept. 1912	36						
1913							
Oct. 1912	42	.....	.....	.....	.0025		
1913							
Nov. 1912	40	.....	.....	.....	.0025	.00023	.00032
1913							
Dec. 1912	45	.....	.0022				
1913							

[1] The figures in this column represent fractions of a gram to the eighth decimal (.00000052).
[2] Alcohol not removed from this tincture.

such different lines. A confirmation of these observations would certainly suggest that careful pharmacological study of digitalis preparations made with different menstrua would not entail a waste of time.

From the Laboratory of Experimental Medicine, ELI LILLY AND COMPANY, Indianapolis, Aug. 26, 1913.

MAGMA BISMUTHI.

BY S. BERTHA MÜLLER, P.D.,
Assistant Pharmacist at the German Hospital, Philadelphia.

In recent years Magma Bismuth has become quite popular, so much so that it was deemed advisable to make the preparation official.

With that end in view several formulas have been proposed and duly tried out, but in our experience have not proved generally satisfactory.

The formulas proposed direct ammonia water to be used to precipitate the bismuth nitrate. This, in our experience, leads to considerable trouble trying to wash the resulting Magma free from the excess of ammonia. It takes a great deal of water to do so and even if one has succeeded in getting the final washings to no longer react with phenolphthalein the Magma itself will always give a strong reaction. To reduce the amount of ammonia water leads to a reaction in the opposite direction, giving a decided acid reaction which causes the gradual solution of the bismuth hydroxide. Furthermore, when the Magma is poured on a strainer for the purpose of washing it, the surface of the Magma very soon develops a metallic coating which certainly points to a decomposition going on and may be due to exposure to air. Unfortunately this is the only way the Magma can be washed because distilled water has the property of causing the Magma to curdle into large flaky masses, taking up considerable water and holding it so that it is utterly impossible to get the Magma to settle in order to wash it by decantation, thus preventing undue exposure to air.

Attention should also be drawn to the fact that the amount of bismuth subnitrate used, results in too thick a Magma. Furthermore, 80 grams of bismuth subnitrate cannot be satisfactorily dissolved in 60 c.c. of nitric acid. It takes 1 c.c. of nitric acid for every gram of bismuth subnitrate to be dissolved.

However, with some modifications the proposed official formula will give satisfactory results. In the first place the amount of bismuth should be somewhat reduced, then ammonium carbonate should be substituted for ammonia water, and lastly, distilled water containing 1–1000 sodium chloride should be used. By using ammonium carbonate the resulting Magma is not nearly so alkaline, it will not react with phenolphthalein but will and should react alkaline toward methyl orange. It therefore does not require nearly so much washing. It only needs to be washed until it is practically tasteless. The use of this small amount of sodium chloride in distilled water prevents the curdling of the Magma, and it therefore can readily be washed by decantation, no strainer being required. After sufficient washing it is allowed to settle to the required volume, which usually takes about a week.

Spigot water can also be used in place of distilled water if it has been previously boiled with 1 per cent. magnesium carbonate for

about 15 minutes, then cooled and filtered and 1–1000 sodium chloride added.

The following formula has been fairly satisfactory:

Bismuth Subnitrate	50.0
Nitric Acid	50.0
Ammonium Carbonate	80.0
Distilled water to make	1000.0

Dilute the nitric acid with an equal volume of water and dissolve the bismuth subnitrate in it, dilute further to 300 c.c. and filter through cotton.

Dissolve the ammonium carbonate in 3000 c.c. distilled water containing 1–1000 sodium chloride and filter.

Pour the acid solution slowly and with constant stirring into the alkaline solution. When the resulting precipitate has subsided, decant the supernatent liquor and wash by decantation until the Magma is practically tasteless, using distilled water containing 1–1000 sodium chloride. Then allow to settle to 1000 c.c.

When tested the Magma should react alkaline toward methyl orange.

BOOKS AS A SOURCE OF DISEASE.

By William R. Reinick.

I do not for a moment want anyone to think that I am endeavoring to prove that books, as fomites, are so dangerous that they should be shunned like the plague, but simply to show that books, especially when greasy or moist fingers are placed upon the pages and covers, are excellent hiding grounds for bacteria, both pathogenic and non-pathogenic, and that the same care should be used as in handling other objects of like character.

Is Such Transmission Possible?

As far as our exact knowledge of books and papers as a source of danger is concerned, we, at the present time, have very little evidence, but what we have proves beyond question, that disease may be contracted by this means. On the other hand there are many reputable physicians who claim that transmission by this means is an impossibility, due to the fact that the organisms could not exist

for any length of time under such adverse conditions. A statement of this character is generally made by one who only has a superficial knowledge of the subject, especially in its biological aspect. The apparatus needed to properly conduct experiments upon bacteria is quite expensive, and generally, the young physician who has just graduated has the time and possesses the enthusiasm to undertake these researches, but not the capital, and then when he has the means, he has so many patients that he cannot spare the time.

Another trouble is the extreme difficulty which arises when one is prepared to study this subject. On account of the great surface covered by the pages of the books, it means a long and tedious series of experiments, and even then, on account of their being invisible to the eye, one is not sure that he has obtained every speck of life that may be on the paper.

The knowledge that we are now acquiring as to the great resistance of these small forms of life to adverse conditions of climate and atmosphere, their resistance to degrees of heat, their wonderful adaptability to rapid changes of environment, food, and their power to remain dormant for a period more or less unknown at the present day, their ability to form a protective coat, which prevents penetration when placed in material that would otherwise destroy them, all these points indicate that we may be on the wrong track in using the present means of eradication. And furthermore, in making our laboratory tests we are forced to isolate the colonies, giving conditions foreign to their natural state of existence, and also the difficulty in separating them into distinct species.

Newman states as follows: "A word may be said here respecting the much-discussed question of species of Bacteria. A species may be defined as 'a group of individuals,' which, however many characters they share with other individuals, agree in presenting one or more characters of a peculiar and hereditary kind with some certain degree of distinctness. Now, as regards bacteria, there is no doubt that separate species occur and tend to remain as separate species. It is true, there are many variations, due in large measure to the medium in which the organisms are growing—variations of age, adaptation, nutrition, etc.—yet the different species tend to remain distinct. Involution forms occur frequently, and degeneration invariably modifies the normal appearance. But because of the occurrence of these, morphological and even pathological differences of environment and physical conditions must have marked effect

upon such sensitive units of protoplasm as bacteria; it has recently been proven that one great reason why modification occurs in pure artificial culture is that the species has been isolated from amongst its colleagues and doomed to a separate existence. One of the most abstruse problems in the immediate future of the science of bacteriology is to learn what intrinsic characters there are in species or individuals which act as a basis for the association of organisms for a specific purpose. Some bacteria appear to be unable to perform their regular function without the aid of others. An example of such association is well illustrated in the case of tetanus, for it has been shown that if the bacilli and spores of tetanus alone obtain entrance to a wound, the disease may not follow the same course as when with the specific organism of lactic acid bacilli, or the common organisms of suppuration or putrefaction also gain entrance. Again, the virulence of other bacteria is also increased by means of association. The bacilli coli is an example, for, in conjunction with other organisms, this bacilli, although normally present in health in the alimentary canal, is able to set up acute intestinal irritation, and various changes in the body of an inflammatory nature."

Among the higher forms of life we have, in a few hundred of years, recognized natural changes, or often brought the change about by artificial selection. Now if a change, quite noticeable, can be made during a period of years, in forms which do not produce more than one or two generations a year, what changes are able to take place, in forms capable of producing a new generation every twenty or thirty minutes, and these changes invisible to us?

Another source of failure to obtain positive results is due to the fact that conclusions are generally arrived at from twenty-four hour tests; and, if there is no result within that period, the experiment is marked negative and the material destroyed.

Very little information of value, to help in deciding whether or not books act as carriers, was received from the various Boards of Health of the United States. A circular letter requesting a list of cases, the source of which was traced to books and papers, was sent to the Boards of Health of each State and forty-one cities. Answers were received from only ten States and nineteen cities, about 30 per cent. of the total number of letters sent.

With these replies no cases were given, although some of the officials stated it to be their belief that diseases were contracted through contact with books, while others ridiculed such a possibility.

Quite a number of physicians have sent me histories of cases, which they have observed during their practice.

The medical and library periodicals are constantly printing notices about disease being contracted from books, and as in the case of the theory of insects transmitting disease germs, at first ridiculed, but now acknowledged to be true by the most skeptical, so are books now passing through the same criticism.

Diseases Claimed to Have Been Traced to Books.

Scarlet Fever.—Dr. J. Allen Palmer, of Erie, Kansas, notes a case of scarlatina developing in a girl, living in a town where there had been no cases of the disease for months, nor had she been exposed to personal contact. Investigation showed that the patient had received a letter a few days previous to the appearance of the rash, from a child living some sixty miles from her, who was just recovering from scarlatina. Another case of transmission was traced by Dr. Howard W. Lyon, of Chicago. In this instance a little girl living in Chicago contracted scarlatina from being allowed to handle a letter just received from a home in Minneapolis, where one of the family had the disease.

Dr. A. Maverick, of San Antonio, Texas, sent the following case: A boy convalescent from scarlet fever read a book from the public library and used as book-marks strips of skin peeled from his hands and feet. Unknown to the physician, the book was returned to the library by a servant of the household with no attempt at sterilization or even removing the pieces of skin. During the next month, two boys in different families who borrowed the book from the library, caught scarlet fever and one died from the disease.

Diphtheria.—Dr. Robert Britton, of Downsville, New York, writes of two cases in 1902, one of the patients dying, and as there were no cases of the disease in the neighborhood, the question arose where had the children contracted the infection. Questioning revealed, that on account of the weather and conditions of the road they did not attend school on March 27, but played in a house having a garret, in which were stored some old school books which had been taken from an old farm-house on this farm—in which in 1860 had occurred six cases of diphtheria, four of which were fatal in forty-eight hours.

Small-pox.—Small-pox is one of the most contagious diseases, and few who are exposed escape infection. The contagion exists in

the pustules, in the fluid of the body, and apparently in the exhalation from the lungs and skin. The dried scales thrown off during desquamation are the most important element in disseminating the malady, and is often communicated, through the medium of clothes, furniture, books, etc., which have come in contact with patients.

Dr. P. A. Jordan, of San Jose, California, states the following: A man, a great reader, continuously used books from a circulating library located in a neighboring town in which there was an epidemic of small-pox, and later developed a severe form of small-pox.

Blood-Poisoning.—Dr. Emericus Karacson, while making a translation of a Turkish Manuscript, in one of the Mosques in Turkey, had his fingers soiled with some of the mould which covered the old musty tomes, and accidentally touched a cut on his face; a few weeks later his face swelled up, causing him intense pain. A quick operation relieved him of this and his face regained its normal size, and he soon resumed his work, apparently in perfect health. About a month later he was taken ill with fever and treated first for influenza, then for typhoid fever. His condition growing worse, a Hungarian physician was sent for, who diagnosed the case at once as blood-poisoning, caused no doubt by the fungi that had entered the patient's system through the abrasion on the face, and he died within a few days.

Venereal Diseases.—That the danger to man from what are called the "social evil" diseases, after exacting a cost in human life and physical disability beyond computation, and the necessity of using means which will prevent its spread, is now recognized, as seen by the numerous societies being formed to furnish speakers and publish literature upon the subject, thus forcing the public to face the question as it has never been done before.

A list of articles found to be carriers of the germs of gonorrhea, the one most likely to be contracted through contact, would include every article of domestic and public use, and even the hands of the unclean and ignorant may transfer the germs to the articles. A number of cases have been traced to books.

Diseases, besides these mentioned, have been named as being transmitted by books, and there is no reason to doubt that the germs of other diseases found on fomites will also be found on books. The bacillus of anthrax, which occurs in cattle, must certainly be found on the leather bindings, as it is frequently transmitted through

abrasions of the hands in cases of those who have the occasion to handle infected wools and hides.

Tuberculosis.—The number of bacilli in the sputum of a person suffering from tuberculosis is enormous. Nuttall estimated that a person moderately advanced in the disease, expectorated between two and four billions of bacilli every twenty-four hours. One having this disease does not at once become helpless, and in the meantime the patient generally spends a great deal of his spare time reading, and as this disease usually causes the one inflicted to cough a great deal, often involuntarily, it is but natural that particles of the sputum will be caught on the paper of the books, ready to be transmitted to another victim.

Dust.—I do not think that enough study has been given to the bacteria found in dust, as far as public institutions are concerned. Careful consideration of the examinations already made of dust from various sources, especially in the industrial trades during the past few years, will show at once that the health is often affected by the impurities found in the air inhaled, and that the purifying of this air is of greatest importance from a sanitary standpoint. Besides the danger from exposure to the so-called diseases, the germs of which are stated to be borne in the air, the pollution of the air by organic and inorganic dust is beyond a doubt the cause of a great deal of ill-health, and death.

An analysis made by Prof. Charles H. Lawall of dust collected by me at the State Library of Florida, at Tallahasse, off of books that had not been disturbed for many years, gave the following result:

" Ash (inorganic material, mainly sand), 54.90 per cent.

" Organic matter consists of much unidentifiable matter, in which, however, could be distinguished microscopically the following: wood fragments, cotton, linen, silk, wool (some of them dyed bright colors), hairs of various kinds, both plant and animal, starch grains, spore and an occasional yeast cell. No evidence was found of arsenic or mercury or other poisonous metals or their compounds, except what might be called a faint trace of arsenic, which was traced by a method so delicate as to detect arsenic in almost any substance from which it has not been specifically removed."

Dr. McFadden and Mr. Lunt seem to prove the paucity of bacteria in very dusty air. The evidence otherwise available is entirely conclusive that the risk to disease infection is much greater indoors than out in the open, where the germs are exposed to the

sunlight, which is a great factor in keeping the germs in an inactive state.

But, besides the danger of infection from inhaling disease germs found in the dust, there is also to be considered that it is the cutting edges of the particles of dust, which when inhaled scratch or cut the delicate air passages leading to the lungs and also the lungs themselves. The finer dust will not, perhaps, act as quickly as the coarser grains, but it means that the evil result will take a much longer time before making its appearance.

It is known that those who spend most of their time in outdoor occupations, generally have better health than those who are compelled to work in factories, offices, etc., and the first thought of sanitary science to-day is the elimination of dust.

It is extremely difficult, in fact almost impossible, to trace many cases of infection on account of the long period between the first infection and the appearance of the disease in a form to demand medical attention.

Dr. Hugh H. Brown, of Washington, D. C., and an assistant, in 1907, moved a large number of books which had not been disturbed for quite some time. Within a few days both contracted severe colds, characterized by distinct bubbling, and a severe cough accompanied by a feeling of compression and pain in the chest, and an exceedingly profuse and purulent expectoration of a deep yellow color the consistency of thick cream. The cold lasted about two weeks.

Vitality of Bacteria.—Before considering the mode of overcoming these organisms, consideration should first be given to their power of resistance to disinfection, sterilization, etc.

Bacteria exist in nature in three states:

(1) As adult or fully-developed and active microörganisms, with all the characteristics of parasites.

(2) As spores or reproductive cells endowed with latent life.

(3) As desiccated germs, whose vital principle had been suspended but not destroyed; which, when placed in a moist and suitable environment, possess the power of resuscitation.

"The air germs," says Professor Tyndall, "differ much among themselves in their tendency to development; there are some which are young and there are others which are old, some dry and some wet. The same water infected by those germs requires more or less time to develop bacterial activity. This explains the difference in the rapidity with which epidemic diseases act upon different persons.

In certain cases the period of incubation, if it can be so called, is long, in others it is short; the difference is the result of the different degrees of preparedness of the contagious matter, and I personally believe that the health of the person infected has most to do with the appearance or non-appearance of a disease."

The length of time that the different pathogenic bacteria can withstand drying varies greatly. Krausz placed bacteria from 48-hour old cultures in books and kept them in the dark at room temperature. He found that cholera lived only 40–95 days and tubercle bacilli 80–103 days. Other investigations confirm his results except in the cases of tuberculosis and diphtheria. Abel found that diphtheria bacilli retained their virulency on toys for six months and this is the length of time that Von Scham gives. Lion and Von Schab both say that tubercle bacilli withstand drying from six to nine months.

The number of bacteria that may be found on much-used books was investigated by Lion. A novel from a public library varied from 250 bacteria per 100 square centimetres on the middle of a clean page to 1,250, 1,875, and 3,350 on the dirty edges. A college atlas showed from 650 to 1,075 per 100 square centimetres; an anatomy book 2,275 to 3,700. The bindings were by far the richest in bacteria, yielding on an average of 7,550 per square centimetre.

As to the pathogenic bacteria that may occur on books, the following investigations are of great interest. Krausz inoculated seven guinea pigs with dirty pieces of paper from much-used books and they all died of peritonitis. The eighteen inoculated with pieces from clean books remained healthy. Du Cazal and Catrin found Staphylococcus pyogenes on an old book in a hospital. Most striking of all are Mitelescu's experiments. He took 60 much-used books that had been in a public library from six months to two years; he cut out the dirtiest parts, soaked them in salt solution, centrifuged the liquid and inoculated guinea pigs with the sediment. Nineteen died of septicemia, and twelve of streptococcus infection. He repeated the experiment with thirty-seven books from three to six years old. Fourteen of the guinea pigs died of septicemia, and fifteen contracted tuberculosis. The damp dirt on the older books was a good medium for tubercle bacilli.

The following abstracts are taken from the report made to the Board of Trustees of the Chicago Public Library upon books in that

library by Dr. W. A. Kuflewski and are of value as showing the germs to be found on books long in use.

These books were selected by Mr. F. H. Hild, Librarian, and Dr. Reynolds, the object being to get the books that were most worn and most soiled, and the examination was made by Dr. Adolph Gehrmann, who reported as follows:

D 2017a From delivery station, 14 years.
19 Cultures from page 57, brown spot—negative.
Cultures from torn places on cover.
(A) Staphylococci and saprophytes.
(B) Negative.

C 7357 Delivery station, 20 years.
Cultures from title page—negative.
Cultures from title page—negative.
Cultures from page 19—negative.
Cultures from page 19—negative.

H 2455c Delivery station, 6 years.
Cultures from top of page 278—negative.
Cultures from leather back—Staphylococcus pyogenes albus.
Cultures from bottom edge of pages—Staphylococcus pyogenes albus.
Cultures from top edge of pages—saprophytes and S. pyogenes.

F 8346c Circulating department, 2 years: Popular juvenile.
Cultures from leather back—negative.
Cultures from top of pages—negative.
Cultures from page 190—negative.

F 494aa Circulating department, 26 years: Popular fiction.
Cultures from spot on page 25—negative.
Culture from leather back—negative.
Cultures from bottom pages—negative.

RR 281 Buck's Cyclopædia, 14 years: Reference book.
Cultures from leather back—1 colony of Staphylococci.
Cultures from edge of cover—1 colony of Staphylococci.
Cultures from dirty page—Staphylococci.
Cultures from clean pages—Staphylococci.

SUMMARY OF RESULTS.

Negative results: 3 books—C 735; 58 346c; and E 494aa.

Cultures from covers showing Staphylococci: 3 books—D 2017a, H 2455c, and 281.

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Cultures from pages showing Staphylococci: 2 books—H 2455c and RR 281.

1

A series of cultures from the hands of two persons in the laboratory were made in the same manner and these showed a few colonies of saprophytes and Staphylococci pyogenes albus. In a general way these cultures were similar to those giving positive results made from the books.

The method employed in making these cultures was to take a few drops of sterile bouillon and with a platinum wire rub it upon the place from which the inoculations were made and then transfer this loop of bouillon to the blood serum boxes used by the department for diagnosis of diphtheria. These were placed in an incubating oven for forty-eight hours. The resulting colonies were examined microscopically.

Control cultures were made on several boxes by first placing the drop of bouillon on the sterile slide and then transferring it to the blood serum media.

In none of the cultures were diphtheria bacilli found. The Staphylococcus pyogenes albus is one of the pus bacteria usually found upon the skin of most individuals. The saprophytes are accidental non-pathogenic bacteria from the air, and are of no consequence.

Dr. Kuflewski states that "after personal investigation and examination of three sets of books taken at random from the shelves of the Chicago Public Library I am prepared to state that I found bacteria in large numbers in all the samples and that each book was more or less infected. These bacteria were in large numbers and were both pathogenic and non-pathogenic—the word pathogenic meaning 'disease-producing.'"

In many instances these bacteria do not harm, not even the pathogenic, because of the resistance of the tissue—being unimpaired—or because of the comparatively small numbers of bacteria which gain access to the tissues; but under favorable circumstances, such as a simple exposure to cold and especially to bronchitis, which is so prevalent in Chicago, a little wound or an abrasion of the surface of the body, a little scratch of the mucous membrane or of the skin, which as we all know is often treated as insignificant and is neglected, may be the means of introduction into the system of the most infectious disease germs. It is well known that a fresh wound absorbs bacteria and their toxins very rapidly.

I have had in my own experience a case in which I satisfactorily proved that a child contracted an infectious disease in the eye, from

the page of a book. Prof. Dr. W. A. Evans, who is an authority, states the case of a person who was infected with typhoid germs from books, which case was established beyond question. I had another case two or three years ago; a gentleman who was suffering from cancer in the roof of the mouth, in which the tongue and lips were also affected, was reading books from public libraries in this city for nearly two years and until I was called to treat him. He had been treated before by the "faith cures" and by the followers of Dowie. This patient was found expectorating minute pieces of his tongue and lips, which were a cancerous tissue, all over the pages of the book he read. That they were cancerous was not only proven by my own examination, but by that of Dr. LeCount, an eminent bacteriologist, who reported to me that the piece of tissue submitted was cancerous, containing cancerous cells.

Of course I prohibited this person from reading any more books from the libraries, and told his wife to be very careful as the disease was contagious.

In my own experiments I had no difficulty in obtaining colonies from the pages and bindings of all of the books examined, and I also obtained cultures of various forms from dust many years old, which according to the text-books, should have been destroyed.

Flies.—These insects are now known to carry germs. In some cases as many as six million have been found on a single specimen. In very few cases are libraries protected by screens; the fly just from a patient suffering from a contagious disease, or off the waste matter in a near-by cesspool, has easy access to the interior of the library, where, alighting upon a binding or page of an open book it proceeds to eject a number of germs with its excreta, or by rubbing its body with its forelegs, shakes large numbers off, which find ready lodgement, especially if the spot where the rubbing takes place is greasy, as is generally the case where a book has been much used or circulated for quite a number of times.

People do not seem able to overcome the vulgar habit of moistening the fingers in turning over the leaves of the books and again placing the finger on the lips each time to remoisten, never considering that each time he is, perhaps, transferring germs to fertile soil for propagation, resulting in sickness later on, or in case of a patient already suffering from disease, especially tuberculosis, helping to inflict another victim with the disease. And we all know that sick

persons, especially in the convalescent stage, spend a great deal of their time in reading books and magazines.

Disinfection.—This process in killing germs in books, although recommended, especially by those who have the disinfectants and the apparatus for sale, may be dismissed as of very little use, on account of the impossibility of the gases penetrating into the interior of the volumes, and in no case, even if the entire surface is reached, will they remove all of the spores.

Sterilization.—Both steam and hot air sterilization are of little value for books, because the first will cause the paper of the books to absorb the moisture, swell and deform the book, and while in the case of hot air sterilization, the heat would, by drying up all the moisture in the books, have the same effect, besides, in the case of books bound with leather, cause the leather to stretch and often break.

The heat also will absorb the moisture and the paper will become dry and brittle, lessening the life of the volume. At present I do not believe, that there is any method which may be depended upon to entirely eliminate the possibility of diseases being contracted through contact with fomites, such as books and the hundreds of other articles in daily use, constantly being transferred to a sick-room, returned and ready for another victim. I believe that some of the State Boards of Health are now beginning to recognize the futility of quarantining and disinfecting. Instead they are spending all their energies in improving sanitary conditions as to the necessity of cleanliness and the proper care of health. If a person using books or any other of the numerous articles named as conveying germs will use precautions as to the degree of cleanliness of the article they handle, and will take the proper care of their health, they need have no fear of contracting any disease by means of a book or any other article.

Suppose that a library did disinfect their books, what claim can they make that the book has no germs, after it has been placed on a shelf next to another book or been handled by a reader or one of the assistants. Dr. A. W. Doty, of New York City, states along the line of using disinfectants at intervals, "I know of nothing in public sanitation which is more farcical than the general or periodical disinfection of books with gaseous disinfectants for the purpose of preventing infection. These agents have no penetration of any account, and I have little faith in them for this purpose. I believe

that the careful dusting of the books and an abundance of fresh air and proper ventilation in a library is all that need be done under ordinary conditions."

He here touches the remedy, cleanliness, in relation to the books, but the same care that should be given to keeping the books clean should also be insisted upon for the employees and readers of libraries and all places where dust may accumulate.

A visit to almost any library will generally show, by placing the hands in back of the books upon the shelves, that there is a great deal of dust lying there. Very few libraries, even those recently erected, have had the vacuum system, which seems to be almost perfected, installed. Instead of making the reader wash his or her hands before using a book, it is very difficult for one to obtain access to the lavatory to wash his hands even if he so desires. In fact, there are some libraries which have no lavatories at all for the public.

Books are often placed on shelves in stacks, poorly ventilated and lighted. The results obtained in the library at Hawaii, whose books were constantly being destroyed by insects while stored in a dark, badly ventilated building, but was almost eliminated when transferred to a well-lighted and ventilated building, prove the value of pure air and sunlight. Not disinfectant plants, but sunlight, fresh air, the elimination of dust, and the proper cleanliness on the part of the employees and readers, is the way, not only to prevent books from becoming fomites, but also the people becoming carriers in this age of prevention.

EHRLICH'S CHEMOTHERAPY.[1]

How His Logical, Systematic Campaign Against Certain Diseases Has Demonstrated the Value of Scientific Methods in Therapeutical Problems.

By Henry P. Talbot.

Chemotherapy has been called "a new science." It should, rather, be regarded as the designation of a scientific field in which therapeutics and chemistry intermingle in the solution of problems involving the principles of both of the older sciences, much as do physics and chemistry in so-called "physical chemistry," which is not, on that account, regarded as a "new" science.

[1] Reprinted from *Science Conspectus*, March, 1913.

Therapeutics is defined as that branch of medical science " which deals with the composition, application, and modes of operation of the remedies for disease." But it has now taken on a somewhat broader, though less exact, meaning, and is understood to include the general administration of medicine, questions of hygiene and dietetics, and much that has to do mainly with the general well-being of the individual. That chemistry must be, as it has been for centuries, inseparable from the study of therapeutics is obvious, and the advance from the simplicity of the theory of Geber, according to which the animal organism was made up of only " sulphur " and " mercury " to our still very imperfect knowledge of the complex changes of physiological processes is, indeed, remarkable. But modern medical and chemical science is not content with the mere alleviation of the ravages of existing disease, that is, with the modifying or assisting of functions temporarily disturbed, but has struck more directly at the root of the trouble by devising means actually to destroy the causative agents and thus arrest the disease, or to render the animal organism inhospitable to these causative agents, as, for example, through the anti-toxins and the methods of preventive medicine in general.

All this had been done even before the advent of chemotherapy. What, then, is new about this combination of scientific effort in two allied fields? Essentially this: It is a logical, systematic campaign against diseases which are caused by the infection of the animal organism by parasites (*i.e,* bacteria or protozoa) by means of chemicals which have not been found by empirical and more or less haphazard methods, but have been synthesized and built up solely for the purpose in hand, and as the result of researches which have called for the highest type of accurate observation and analytical reasoning for their execution. In this way it has been found possible to devise means by which the animal organism can be sterilized with respect to the parasites in question, and the consequent symptoms of disease can be arrested.

The development of this field is due almost entirely to Professor Paul Ehrlich, of Frankfort, and his co-workers. Dr. Ehrlich was educated as a physician, but has now become also one of the most accomplished and able investigators in the field of synthetic organic chemistry. A conception of the significance of his work can, perhaps, be best obtained by noting important phases in its progressive development.

More than thirty years ago Ehrlich began using coal-tar colors in his physiological studies, employing them as stains for preparations to be examined under the miscroscope. It is, of course, now commonly known that certain dye-stuffs appear to have a selective affinity for certain tissues of the body, or for certain parasites when residing within it, and these stains are in every day use by the pathologist. But it was not so thirty years ago, and Ehrlich first found that a dye-stuff known as methylene-blue, and its congeners, were the only colors which would stain live nerve tissue, and drew from this the important inference, which is at the basis of chemotherapy, that this was because of a particular receptivity for these dye-stuffs on the part of these tissues or parasites. It is easy to understand something of the importance of this use of these stains, or dyes, if it is recalled that the changes produced in the individual cells or tissues by drugs are not detectable even under the microscope in most cases, and that it is only through these stains that a knowledge of what has actually happened can be even approximately learned.

Ehrlich concluded from his observations that it was probable that, since these tissues and parasites possessed this receptivity for these specific bodies, there must be some definite effect produced as a result of the combination, if combination it were, and proceeded to conduct investigations in this direction. After some time these researches were rewarded, and in 1890 Ehrlich and Lappmann published a paper on the pain-relieving properties of methylene-blue, and, later, Ehrlich and Guttmann found that the same dye was fatal to one type of the plasmodium, the parasite which causes malaria. As the latter field of investigation, that of the effect upon parasites, appeared very promising, they turned their attention to a particular class of parasites known as trypanosomes, because these could be more easily studied by the inoculation of mice.

The disease-producing parasites are sometimes of vegetable origin, as the bacteria, and sometimes of animal nature, as the protozoa. The trypanosomes are worm-like bodies, somewhat larger than bacteria, belonging to the animal class, and the diseases which they produce prevail most generally in tropical countries. Of these diseases, surra, most generally known in India among cattle, dogs and camels; nagana (tsetse-fly disease), known in Africa among animals in general; and mal de cadaras, known in South America among horses, are typical, while man is also attacked by the sleeping

sickness in the tropics. The scourge of syphilis is produced by a parasite known as the spirochete, which is closely allied to the others named, although it is still undetermined whether its nature is animal or vegetable. As will be seen, this particular disease has been found to be one of the most amenable to treatment.

As a result of his researches, Ehrlich formulated a theory regarding the behavior of the cells of living tissue, or of parasites toward foreign bodies. He conceives them as made up of a central "dominant body," which throws out "sidechains," to which he later gave the name receptors. These are of variable character, some being nutrient receptors, and others chemo-receptors, that is, receptors or certain definite chemical elements or groups of elements, known in chemistry as radicals. In a crude sense, the receptors may be likened to locks, and the nutrient or chemical bodies as keys, each fitting a particular lock, as, for example, the dyestuff methylene-blue already mentioned. The combinations thus affected may be beneficial to the cell, as in the case of the nutrients, or they may result in the poisoning and death of the cell, as in the case of the methylene-blue when brought into contact with the type of plasmodium referred to above, or quinine for plasmodia in general, a specific remedy for malaria discovered by empirical research.

Ehrlich and his co-workers, with extraordinary skill and industry, prepared several hundred dye-stuffs, studying the varying effects of alterations in chemical structure, each new compound having been logically selected as the result of laboratory tests of its parasiticidal efficiency. Of all these, very few finally withstood severe tests, possibly not more than ten in all, but the fact was established that it was possible in certain cases to sterilize the animal organism with respect to parasites, by this means, without, at the same time, poisoning the animal itself. They were also able to establish certain principles as to the chemical structure of the dye-stuffs most likely to be effective. They encountered, however, many difficulties. A dye which would attack and destroy a given parasite in a particular animal would not always do so in another species. Symptoms of disease would sometimes recur after varying intervals, and the parasites would then often exhibit peculiar resistance to further attack.

While these researches were still in progress, Uhlenmuth and Salmon published an account of instances of marked success in the destruction of the spirochete of syphilis, and the arrest of the disease, by the use of an arsenical compound known as atoxyl. Secondary

and seriously harmful effects to the patients were, however, the consequence of this treatment, but the parasiticidal properties of this compound were so marked that Ehrlich turned his attention to it, in an attempt to so modify its effects upon the animal organism which was harboring the parasites, that its curative power might be made available.

The task was by no means a simple one. He first established the composition of the atoxyl as a para-amido-phenyl arsenic acid. The vast amount of work already done with the dye-stuff indicated certain lines of probable success, which, nevertheless, was only attained on the synthesis of the six hundred and sixth organic compound by Ehrlich and Kata, sometimes known as "606," and now designated salvarsan. Chemically it is dioxy-diamido-arseno-benzol, in which arsenic is associated with structural groups akin to those found in the dye-stuffs. A later preparation "914," known as neo-salvarsan, is said to be a combination of a salvarsan with sodium formaldehyde sulphoxalate, which is designed to overcome a certain difficulty in administration of the salvarsan, due to acidity of its solutions.

Ehrlich assumes that the parasite of syphilis, the spirochete, possesses among others, arsenio-receptors, and that through the combination with this arsenic compound the parasite is poisoned and dies. Ehrlich claims that in more than twelve thousand cases in which this drug has been administered by him, no single case of poisoning has resulted. The administration of the drug, which is intravenous, or intramuscular, requires, however, considerable skill and care. The treatment with salvarsan is often combined with that of mercury. There seems to be no doubt that this preparation exerts a specific and destructive action upon the spirochete, and has already resulted in the alleviation of an enormous amount of suffering (often hereditary and undeserved) from this dreadful scourge. It is still too early to make final statements as to the permanence of the cures affected although there is much reason for hopefulness. It should, however, be noted that this chemotherapeutic treatment, unlike the anti-toxin treatment for certain other diseases, does not at all produce immunity from later infection from the same disease. Indeed, there is some evidence to show that cases of re-infection are distinctly harder to treat successfully than those of initial infection. The cure of advanced cases of the disease naturally, presents greater difficulties, because of secondary disturbances of the vital organs, but many of these have been materially alleviated.

The progress made in the chemotherapeutic treatment of diseases produced by other trypanosomes, notably that of the " sleeping sickness," has been less marked up to the present.. Something has been gained, but no specific drug comparable with salvarsan in its efficiency has yet been found.

It is, however, recorded that in Surinam a hospital was established to treat cases of another tropical disease known as the yaws. In the course of eight days three hundred and twenty-eight cases were admitted, and at the end of fourteen days the last patient was discharged, cured, and the hospital had to be closed.

In another field the work of Ehrlich has led to procedures which are of the greatest promise in the study of the processes involved in the progress of medical and physiological research, namely, so-called " vital staining." By means of the injection of dye-stuffs into living organisms, it is possible, because of the selective receptivity of certain tissues or parasites, for a particular color, to trace the movement of bacilli, and to watch the changes which they occasion in the living organism itself. The same procedure is employed in the study of healthy tissue.

To Ehrlich's clear, analytical mind, exceptional executive ability, fine technique, and extraordinary industry is due not only the procedure by which certain particular diseases may be arrested, but a splendid example of logical attack upon other similar problems, which offers great promise for the future, even though, as in the case of the anti-toxins, one marked success may not be at once followed by others of equal moment. He has demonstrated, in a way which cannot be detailed in the scope of this article, that the test-tube experiments made in the laboratory with a particular drug upon a special parasite cannot be alone relied upon as an index of the effect upon it of the same drug when it is harbored by the living organism, since the action is essentially modified by that organism, and he has advanced theories which at least help in the understanding of the possible reasons for the variations in behavior thus observed. Even though Ehrlich's chemotherapy may not be, in an exact sense, a " new science," it must be acknowledged to be a most fruitful and helpful combination of the principles of two well-recognized and time-honored sciences for the benefit of mankind.

OIL OF SANDALWOOD.[1]

By E. M. Holmes.

The gradual, but steady, increase in the price of sandalwood oil during the last few years has naturally given rise to enquiries concerning its cause. Neither the growing use of the oil for medicinal purposes, nor the large demand for the wood in India and China, can sufficiently account for it. There is, however, a possible cause that has apparently not received the attention it deserves from merchants in this country. During the last 30 years or more, *Lantana* and *Casuarina* plants have been introduced into sandalwood plantations with the idea of their shade helping the growth of the young sandal plants, and it appears that concurrently with a diseased state of the Lantana, the sandal plants have become affected with what is known as the spike disease.

A most interesting account of this disease is given by Mr. F. S. Mason in the *Pharmaceutical Journal* in 1903 (May 30th, p. 756), which gives an excellent idea of the character of the disease, and of the extent to which the plantations are affected. One remark in this paper is well worthy of notice, viz., that "within five years it has swept whole tracts of country, and unless some means can be devised to check its ravages, it is only a question of time for the plant to become very rare, if not extinct." So convinced was the Mysore Government of the importance of finding a means to check the disease, that in 1907 the Maharajah of Mysore offered a prize of 10,000 rupees to anyone who could discover the cause of the disease, and devise a curative treatment for it. But although the offer remained open until 1910 no one succeeded in winning the prize.

The cause of the disease was investigated on behalf of the Indian Government by Mr. Barber and Dr. Butler, and they came to the conclusion that it was not due to any animal or vegetable parasite, but was connected with the disc-like suckers at the extremities of the roots of the sandalwood tree, by which it attaches itself to the roots of other plants and obtains nourishment from them (*Indian Forester*, xxxiii, 1907, p. 199). That no curative means of arresting the disease has yet been devised is evident from

[1] The *Perfumery and Essential Oil Record*, June, 1913, 161.

a statement published last October in the same journal, to the effect that the disease still continues with dire results, and that in two districts alone some 70,000 sandal trees had to be uprooted.

In order to obtain an idea of the probable cause of this disease it is necessary to pay some attention to the life history of the plant, so far as this is known. As already mentioned, the sandal tree is a root parasite, obtaining its food by means of suckers, which it attaches to the roots of other trees. It has been ascertained by Rama Rao that there are at least 144 species of plants which the sandal tree attacks in this way, as proved by experiment with sandalwood seedlings, and he gives a list of 252 plants which are found growing near or with the sandal tree, but are as yet not known to be utilized as a source of food by this tree. It does not appear to be equally nourished by all of its host plants, and the condition of the tree depends upon the vigorous and healthy state of its host. Thus it is known that a plant on which it will thrive in one district fails to keep it in a healthy state in another, where the conditions are unsuitable to the healthy growth of the host plant. This requirement of the sandalwood tree is well shown by an observation recorded in the *Indian Forester,* (xxxl, p. 191), that when a trunk of *Heptapleurum* was cut down, the sandal plant attached to its roots began to wither, but when new shoots formed on it the sandal plant began to revive. The sandalwood tree sends out roots for 150 feet or more, and therefore requires a comparatively loose and well-drained soil which the roots can easily penetrate and spread in. In a natural state it flourishes at an altitude of 1500 to 4000 ft., the best yield of oil being obtained from trees growing between 2000 to 3500 ft., on loose volcanic soil mixed with rocks, and preferably ferruginous in character. It requires to be shaded by thickets above which it can form a head of leafy branches.

Although in rich soil it grows more luxuriantly, less scented wood is formed, although, as the tree furnishes more wood, the proportion is about the same. It is considered that the richness of the wood in oil depends more upon elevation and exposure, since, although the tree grows luxuriantly at 700 ft., the wood is said to be totally devoid of scent at that altitude (*Indian Forester,* xxvl, pp. 1–50, 1900).

The experiments made by Rama Rao indicate that the physical conditions of soil and drainage affect the development of the root-branching system. The soil needs to be well drained, as the seed

rots in soil where stagnant water is present, more readily than in most plants.

The seed of the sandalwood tree germinates freely in the thickets where the tree grows, within a month of being sown, although germination may occur any time during three months or longer, but if the seed germinates in open ground where it does not meet with other roots, the seedlings soon wither and die. The young plants for plantations must therefore be raised by planting them with other plants on whose roots the seedlings can feed as soon as they have exhausted the nourishment of their own seed lobes, which lasts for about two months. The seeds are therefore planted in short wide tile tubes resembling drain pipes, but shorter, so that the young seedlings can be planted out without disturbing their root attachments. This planting out is done when they are about 4 ins. high or rather more than a year old. If allowed to grow larger there is likely to be injury done to the roots in planting them out. After planting out, the seedlings require to be gently but copiously watered until well established.

Experiment has shown that the best plants to grow with the seedlings are *Pongamia glabra, Gossypium arboreum, Albizzia Lebbek* and *Cleistanthus collinus.*

The seedlings need protection from animals, as the foliage of the sandalwood plants proves very attractive to them. Cattle and goats will greedily eat the foliage whenever they see it, and deer will leap over the obstructing bushes to get at it, and hares will creep through the thicket to reach it.

As the seedlings in a wild state reach only a height of 3 ins. the first year, and 12 ins. the second year, they are easily destroyed. It is only in the fifth or sixth year they appear above the surrounding bushes and form a leafy head. At this time the stem is about 1 in. in diameter.

It takes 18 to 25 years before the tree is fit to yield oil. With respect to the spike disease, the trees attacked by it present the appearance of being dead, but on careful examination many leaves are seen to be scattered over the tree at the end of the stiff branches, but they are very small, and form small terminal tufts, hence the name "Spike" disease. The shoots are found to be full of starch, indicating that the plant has not been able to utilize its stored-up nourishment. The disease is pronounced to be infectious, because

all sandal plants, in plantations where it occurs, have died, whilst solitary trees are still thriving.

From the above facts, recorded by various observers, it becomes evident that the sandalwood tree requires plenty of room so as to be able to select vigorous hosts to feed it; that it requires soil porous enough to enable its roots to spread readily, and that, therefore, if too closely planted, it may easily be starved, especially in hard or heavy soil. The fact that isolated trees thrive in a natural condition also indicates that the disease is one of mal-nutrition, whilst the presence of starch in the withered shoots indicates the absence of a suitable enzyme to transform it into soluble food.

Apparently no attempts have as yet been made to ascertain the chemical constituents that the tree contains, and therefore needs, although Peterson (*Pharmaceutical Journal* (3), xvl, page 575) found that Macassar sandalwood was rich in iron (7.5 pc) and contained traces of manganese. The latter metal is believed to be connected with the activity of enzymes, and it is possible that a deficiency of it in the soil may injuriously affect the growth. Research is also evidently necessary to ascertain if the tree selects one ingredient for its nourishment from one tree and other ingredients from other species, as it is well known that certain enzymes can split up other bodies than those on which they usually act.

There is evidently much to be done before the cause of the disease and the means to prevent it can be ascertained.

Regarding the subject from the commercial side, the possibility of other sources of sandalwood suggests itself. The world's supply of sandalwood oil is at the present time chiefly derived from the trees grown in Southern India, only a comparatively small quantity coming from the Islands of Timor and Sumba via Macassar. The yield from Mysore last year was 2469 tons of sandalwood, exclusive of chips and sawdust. The average price, including chips and sawdust, was 471 rupees as against 461 rupees per ton during the previous decennial period.

The only other oil that at present competes with the East Indian sandalwood oil is that of *Amyris balsamifera* L., a tree belonging to the natural order Burseraceæ, the wood of which is imported from Venezuela, and is known in Europe as West Indian sandalwood. It competes, however, only in medicinal use, not in perfumery.

Of the 20 or more known species of Santalum, which are dis-

tributed over Asia, Australia, New Caledonia and Polynesia, several were rendered almost extinct by the ruthless destruction of the trees during the first half of the last century, and are not now available in quantity for commercial purposes. These include *S. Freycinetianum,* Gaud., of the Sandwich Islands, *S. Hornei,* Seem., of Eromanga, *S. insulare,* Bert., of the Marquesas and Dociety Islands, and *S. Yasi,* Seem., of the Tongo Islands, and *S. Austro-Caledonicum,* Vieill., of New Caledonia. The wood of these trees was chiefly collected for the Chinese market, and not for the distillation of oil. None of these trees, so far as is known, yields an oil equal in fragrance to that of *S. album.*

A log of wood of *Santalum Yasi* from the Indian and Colonial Exhibition was distilled by Mr. C. Umney in 1886, and a sample of the oil sent to Messrs. Schimmel and Co., who considered it inferior both in perfume and therapeutical effect to that of Santalum album. The yield appeared to be 6½ per cent., although the real percentage might have been less, as an unusual amount of water separated from the oil in the winter weather.

Of the trees yielding sandalwood in Australia, some of which were formerly classed in the genus *Santalum,* the oils are known only in a few cases. That of *Fusanus spicatus* R. Br. (formerly *Santalum cygnorum*) or West Australian sandalwood oil, is distilled to some extent in West Australia, but is considered by Gildemeister and Hoffmann to have an unpleasant resinous odor, and not fit to be used as a substitute for East Indian sandalwood oil. It is, however, the nearest to the true sandalwood oil, and contains 75 per cent. of alcohols, which have, however, not been positively identified with santalol, but owing to the small yield of oil (2 per cent.) and the expense of labor in Australia, although the tree is fairly plentiful, it cannot compete with the Indian oil. That of *F. acuminatus* R. Br. (formerly *Santalum Preissianum* Miq.) known as South Australian sandalwood, yields a vivid cherry-red oil, from which crystals separate out on cooling. It has a different, somewhat rose-like odor, and a different composition and specific gravity to that of East Indian sandalwood. *Exocarpus latifolius* R. Br., a West Australian plant, may perhaps yield some of the West Australian sandalwood oil, but there is no evidence that it yields an oil resembling that of true sandalwood.

Several fragrant woods are known under the name of sandalwood in other countries; the wood of *Osyris tenuifolia,* Engl., a

native of Kilmandscharo, in East Africa, has been imported into Germany under the name of East African sandalwood. The oil was described in 1908 as being bright brown in color with an odor intermediate between that of vetivert and gurjun balsam, but quite different from sandalwood (Pflanzenweldt Ost. Afrika C. 167, Schimmel's Report, November, 1908, p. 109).

The Madagascar "Sandalwood," of which the native name is apparently "Hasoranto," is exported from Tamatave in the North of Madagascar to Zanzibar, and thence to Bombay, where it is known as taggar wood, and is largely used as a cheap substitute for sandalwood for funeral pyres. The wood is of a dark brown color, and yields a dark-colored thick oil, with an odor slightly resembling sandalwood, but which for medicinal or perfumery purposes could by no means be used as a substitute for it. Its botanical source is unknown, but is supposed to be a Lauraceous tree.

New Zealand Sandalwood.—The wood of *Olearia Traversii,* F. Muell, was exhibited at the International Exhibition in 1886 under the name of bastard sandalwood. It belongs to the Family of Compositæ, but nothing appears to be known of its oil.

Cochin China Sandalwood.—This is ascribed by Baillon to *Epicharis Loureirii,* Pierre, Fam. Melaceæ, but I have not seen a specimen.

Guiana Sandalwood.—The oil has already been described (*P. & E. O. R.,* 1911, p. 79). Dr. Giessler, of Leipzig, is of opinion that the oil is probably derived from three species of the genus *Acrodiclidium,* or *Ocotea* (Schimmel's Report, October, 1911, p. 82). It does not resemble sandalwood oil in odor and is not known to do so therapeutically.

Ibean Sandalwood.—The wood of *Brachylana Hutchinsii,* Hutchinson (Family Compositæ), is known under this name. The tree grows near Nhairobi and in forests near the coast at an elevation of 5000 to 6000 feet. The timber is white, hard, easily worked, and scented when freshly cut, and is not subject to the attacks of white ants. The native name of the tree is "Muhugu." It does not appear to have been exported as yet, the tree being only described three years ago in the Kew Bulletin, 1910, p. 126. The plant is illustrated in the Icones Plantarum, 292a.

It is obvious, therefore, that at present there is no oil known that can altogether take the place of sandalwood oil, and until a

means of combating the spike disease has been discovered and the best method of cultivation of the tree has been ascertained, the price of sandalwood is likely to rise, especially since it takes from 18 to 25 years for the tree to arrive at maturity and to grow scented wood.

The chemical constitution of the oil does not hold out much hope that it will be an easy matter to produce it synthetically, for even if santalol can be produced from piperidine, there are evidently other constituents that go to form the odor of the oil, and unless these can be ascertained it is not likely to take the same place in perfumery or medicine as the oil distilled from *Santalum album*.

ABSTRACTS OF SOME PAPERS READ AT THE 1913 MEETING OF THE PENNSYLVANIA STATE PHARMACEUTICAL ASSOCIATION.

By John K. Thum, Ph.G., Philadelphia, Pa.

What is the Quality of Pancreatin on the Market?

By Charles H. La Wall.

An examination of some pancreatin by the author disclosed the interesting fact that it was adulterated with powdered malt. Of course this raised the starch converting power, and, as the author states, as this test is the only one applied sometimes and as the general appearance of such a sophisticated sample is normal, a more than superficial examination of pancreatin is necessary to insure good quality.

Sterilization in Pharmacy.

By A. Parker Hitchens, M.D.

The author in a very interesting and illuminative manner describes the possible purposes of sterlization in pharmacy and gives in detail the various methods which have been found to be of value.

Crotalin—Collection, Preservation, Chemistry and Action.

By Walter Rothwell.

Attenuated snake venom, obtained from Crotalus Horridus, commonly known as "rattlesnake," has obtained some vogue in recent years in the treatment of epilepsy. The author briefly de-

scribes the method of obtaining the venom, its preservation, chemistry, and action. It is given hypodermatically and its action is to increase the time of the coagulation of the blood.

The Detection of Cane Sugar in Honey.

By Charles LaWall, Ph.M.

The author concludes that it is impossible to detect added cane sugar in honey by means of a qualitative test; being present normally in small amounts its quanitative determination is preferably accomplished by means of the polariscope. Invert sugar is the kind usually added and can be easily detected in honey that has never been heated.

Oregon and Canada Balsam of Fir.

By J. G. Roberts and M. M. Becker.

The writers state that because of the scarcity of Canada Balsam of Fir for the last year or two a suitable substitute is desirable. And as a substitute Oregon Balsam of Fir is offered to the trade. As is well known this product closely resembles Canada Balsam of Fir.

Finding that the literature on Oregon Balsam contained little information the authors obtained some balsam from a known source and endeavored to obtain data as to tests for identity and purity.

It differed in the main from Canada Balsam in viscosity, solubility in alcohol, and in response to the magnesium oxide test. The Oregon Balsam is thinner; it is completely soluble in alcohol in contradistinction to the official balsam which yields a turbid solution. Canada Balsam when mixed with 20 per cent. of its weight of magnesium oxide previously moistened with water, becomes solid. The Oregon does not solidify even when mixed with 60 per cent. of its weight of magnesium oxide. It was also noticed that the Oregon Balsam does not dry as readily as the Canada Balsam, a quality which renders it inferior to the latter for microscopical work.

Socotrine Aloes.

By C. J. Denneby.

The author remarks that although the United States Pharmacopœia definition of aloes is broad enough to allow recognition of all varieties of genuine aloes yet it neglects to describe some samples

as imported. It is often received in barrels in a pasty condition, containing nearly twice the amount of water permitted by the U. S. P. It is further remarked by the author that when in this condition the only recourse is rejection of the shipment as abnormal as to its physical appearance, or, it being satisfactory as to identity and purity, to dry so that sample is of proper U. S. P. quality. A tabulation of five samples is given; all contained twice the quantity of water allowable; they also failed to pass the alcohol test for limit of gums, dextrins and impurities. While Kraemer and others state that aloes should not yield more than 4 per cent. of ash all of these samples were slightly higher. As is well known and has been for some time, no aloes is obtained from Socotra.

The Microscopic Examination of Ointments.

By Fritz Heidlberg and Chas. E. Vanderkleed.

The value of an ointment, the authors state, consists mainly in the fineness or subdivision of the active ingredient suspended in the vehicle. And to properly determine when the ointment has been manipulated long enough for the active ingredient to be uniformly and evenly divided they advise the use of the microscope. They state that this is the only satisfactory way to tell whether uniform results have been obtained. They also give their technic for preparing slides for this purpose and illustrate by showing micro-photographs of mercury ointments.

BOOK REVIEWS.

Digest of Comments on the Pharmacopœia of the United States of America (8th Decennial Revision) and on the National Formulary (3rd Edition) for the Calendar Year Ending December 31, 1911. By Murray Galt Motter and Martin I. Wilbert.

The foregoing title, known also as Bulletin No. 87, Hygienic Laboratory, needs little introduction to the progressive members of the pharmaceutical profession. It speaks for itself. It is sufficient to say that the literature covered in this review embraces matters that must, if thoroughly and painstakingly studied by the

two revision committees, result in the publication of a Pharmacopœia and National Formulary that will be regarded as authoritative and the last word in pharmaceutical matters.

References to the great mass of literature consulted is complete in every respect and comments relating to the legal status and development of pure food and drug laws, scope, analytical data, clinical tests, biologic products and vegetable drugs are abstracted with the main points of the papers brought out. This is as it should be, as it enables a worker to see at once if a reference is worth while consulting.

It is particularly gratifying to note that references of a practical nature in regard to pharmaceutical preparations and suggestions as to their improvement, both as to formula and method of preparation, are much in evidence.

The "digest" also places at the disposal of the revision committees references to all literature pertaining to international standards. Every decade brings us closer to a realization of the fact that the question of unification of pharmacopœial preparations is becoming a matter of supreme importance. Rapid means of travel and communication are largely responsible for this.

Foreign Pharmacopœias always bring forth considerable comment and criticism from workers and experts from various parts of the globe and last year was no exception. The collaborators of the "Digest" make this fact plain in their references to literature that comments on the German, Russian, Italian, French, Swedish, Swiss, Austrian, Japanese, Dutch, and British Pharmacopœias and the British Pharmaceutical Codex.

Part III of this Bulletin is devoted to a most comprehensive review of the literature relating to comments on official articles 504 pages being required to show what has been said and done in this field of endeavor, and also illustrating what a tremendous amount of reading the preparation of this valuable government publication required for its completion.

JOHN K. THUM.

THE PROPAGANDA FOR REFORM IN PROPRIETARY MEDICINES. Reprinted from the Journal of the American Medical Association. Eighth Edition, 1913.

There are many people who take as gospel truth anything they see in print. There are a great many other people who, while they

know better than to do this, are unable to discriminate and so are almost as easily led as the others. Then there are many people afflicted with some ailment, or think that they are, who clutch, like a drowning man after a straw, any statement which seems to bear upon their case.

To satisfy the "needs" of people like these there is a host of firms who manufacture remedies for every conceivable trouble, and to eliminate the need of having a physician they include in their packages circulars which purport to give complete directions of use. So extraordinary are some of these statements that anyone even only very superficially acquainted with the facts would prick up his ears at hearing them. But not so with the gullible public. The more extreme the statement, the more absolute dependence they place on the product.

Truly, this proprietary medicine venture is no more than a psychological game between the manufacturer and the public, only the public is not aware that it is playing the game. Here are some of the psychological weapons the manufacturer has at his command:

1. As one bows down to a man who is well dressed and imposing in appearance, so one worships an ordinary drug or food (or even a worthless one) when it is clothed in a dignified name.

2. As the average illogical mind believes that what comes after must be due to what goes before, the deduction is easily made that if a person recovers after having made use of some remedy, the remedy deserves the credit. This is termed the *post hoc, ergo propter hoc* argument. The folly of course lies in the fact that in the great percentage of cases the patient would have recovered without any remedy.

Yes, the Propaganda for Reform in Proprietary Medicines, which is a bound volume of reprints, might well be called "A Study in the Psychology of Advertising Worthless Products." A former book of reprints entitled "Nostrums and Quackery" is relative especially to those nostrums which are exploited only—or chiefly—to the public. The volume under consideration, however, relates to those products which are exploited to the physician and includes also some of those in the other volume where there seemed to be an "overlapping."

Some 120 proprietaries are considered, the schemes by which they are foisted upon the public through the medical profession are discussed with numerous reproductions of illustrations of advertise-

ments, and chemical formulas and therapeutic properties are given.

A striking feature is the prominence which must be taken by the products of large well-known manufacturing houses who are making a mighty good thing out of the credulity of the public with no regard to the ethics of the profession.

A. K. LOBECK.

ARBEITEN AUS DEM PHARMAZEUTISCHEN INSTITUT DER UNIVERSITÄT BERLIN, by H. Thoms, v. 10, including the work of the year 1912, Urban & Schwarzenberg, Berlin, Wien, 1913, 220 pages, with two illustrations.

This volume like the ones preceding it reflects the work done in the Pharmaceutical Institute of the University of Berlin, by Prof. Thoms and his associates, and includes a total of 35 contributions, under five general headings: 1, Contributions from the division for the examination of drugs, specialties and secret remedies; 2, reports on organic chemical work; 3, microchemical work; 4, reports from the division for the examination of foods and technical products of the Colonies; 5, general discussion. The whole is followed by an index of four double column pages. The first section of the book includes a systematic review of the new remedies introduced during the year 1912, and reports the analytical examination of a number of proprietary preparations. The phytochemical work reported in this volume includes observations on the production of menthol in Germany and in the German Colonies, and an examination of the seed of *Strychnos kongofera* for strychnine. Lenz discusses the production and use of microchemical reagents in a paper covering eight pages, and Thoms, in a very comprehensive paper, reviews the problems of pharmaceutical education in Germany and other European countries.

Altogether the volume is well up to the high standard that has been established by those preceding it and the renewed energy with which the work on so-called new remedies is being prosecuted bodes well for the general progress of pharmacy along satisfactory lines.

M. I. W.

ARBEITEN AUS DEM PHARMAZEUTISCHEN INSTITUT DER UNIVERSITÄT BERLIN, herausgegeben von, Prof. Dr. H. Thoms.

This publication, the tenth annual volume, consisting of 220 pages, presents a record of the work accomplished during 1912 at

the Pharmaceutical Institute of the University of Berlin under the direction of Dr. H. Thoms, the Director.

It also gives evidence that the German pharmacist, acting through this pharmaceutical institute, is alive to the need of protecting the medical profession and the public against fraud, secret medicines and mendacious advertising. Here, in our own country, the pharmacists have been so busy worrying about price protection on nostrums and telephone rates that the medical profession took the bull by the horns, so to speak, and through its national organization, the American Medical Association, organized a permanent committee, and named it the Council on Pharmacy and Chemistry. What this council has done since its organization is known to all progressive pharmacists. And its efforts for better things are surely showing results. One has but to glance over the proceedings and reports of some of the medical and pharmaceutical societies to realize that we are at the dawn of a new era as to things pertaining to these two professions.

The investigations of the laboratory workers of this German institution covered a wide field in the domain of synthetic chemistry, particularly as regards the output of the dye houses of that country, specialties of all kinds, and secret remedies and nostrums of all kinds.

Under the classification of Analgesics, Antipyretics, and Antirheumatics, considerable attention is given to such chemicals as Melubrin, one of the more recent antipyretics, said to be useful in rheumatism and resembling in its effects the salicylates, chemically it is sodium-phenyl-dimethyl-pyrazolon-amido-methan-sulphonate; Atophan, said to be useful as an antirheumatic in so far as it aids in the elimination of uric acid and chemically known as phenyl-quinolin-carboxylic acid; Novatophan a modification of atophan and tasteless while the latter is bitter; Aspirin Soluble which is the calcium salt of acetyl-salicylic acid; Luminal, a sedative and hypnotic, the chemical name of which is phenylethylmalonylurea; Brophenin, a combination of bromine with phenetidin and chemically known as bromisovalerylamino-acetate-p-phenetidin; many others too numerous to mention are also considered.

Besides giving considerable space in this publication to the investigation of products (Kolonialprodukte) from the German colonies, both as to their chemistry and pharmacognosy, there also appears an exposure of some of the nostrum emmenagogues found

on the German market. One of these consisted of small quantities of oil of cinnamon and cloves in 12 per cent. of alcohol. For two ounces of this wonderful and efficient (?) preparation the modest sum of one dollar was asked. Another, called "Menstruationpulver" consisted of a very poor quality of powdered Roman Chamomile, and for the small (?) sum of seventy-five cents the buyer received a package containing 35 grammes.

An interesting report is given of an examination of a fixed oil sent to the Institute by a German missionary pastor from Venezuela. This oil is used by the Indians in the region of Orinoco as a remedy in the treatment of tuberculosis. The results are reported as good. This oil is yellow in color, slightly cloudy, and in odor and taste somewhat resembling olive oil; at room temperature fluid; on cooling there was separated a small mass of fatty acid which, on warming, disappeared. At 12° C. the oil congealed to a soft butter-like mass. It was miscible in all proportions with ether, chloroform, petroleum benzine, benzol, and carbon disulphide and on the contrary immiscible with absolute alcohol and glacial acetic acid. On the addition of HCl and furfurol no red coloration appeared. The test for cotton-seed oil by the addition of sulphur and carbon disulphide gave negative results. The constants were ascertained in the usual manner and found as follows:

Specific gravity at 15° C.	0.9125
Acid number	4.46
Saponification value	200.45
Iodine value according to Hübl after 2 hours	69.9
Iodine value according to Hübl after 6 hours	71.0
Unsaponifiable constituents	0.48 per cent.
Refractometer number in a Zeiss butter-refractometer at 25°.	59–60
Optical rotation in 200 ccm.-tube	0

The oil also gave the reaction for elaidin. Hehner's method for the separation of the fatty acids was used and the melting point of these was found to be 30.31°, the congealing point 22° and the saponification value 195.5. The fatty acids also gave an iodine value of 75.25. After recrystallization from alcohol twice, the elaidic acid showed a melting-point of 51°. Experiments on mice proved this Ceje-Öl, as it is termed, to be non-toxic. Whether it will be of any more value than other better-known fatty oils in the treatment of tuberculosis remains to be proven clinically.

As one reads through this volume, depicting the work done at this institute, the impression is gained that the aim of the workers is the scientific one, the desire for the *truth;* the truth about those remedies for which there may be a legitimate use and which are more or less ethically introduced, and the exposure of those remedies which are secret in composition and for which extravagant claims are made. JOHN K. THUM.

"A HANKBOOK OF USEFUL DRUGS." A selected list of important drugs suggested for the use of teachers of materia medica and therapeutics and to serve as a basis for the examinations by state medical examining and licensing boards. Prepared under the direction and supervision of the Council on Pharmacy and Chemistry of the American Medical Association. Press of the American Medical Association, 535 North Dearborn Street, Chicago, 1913.

It does not require the gifts of a seer or the abilities of a prophet to venture the opinion that this rather diminutive volume of 167 pages is destined in the near future to have a decidedly far-reaching influence on the teaching and on the practice of therapeutics and, consequently, is designed to have an equally important bearing on the future development of pharmacy and the efficiency of pharmacists generally.

Conscientious students of medical economics have long appreciated the waste of energy, money and even life resulting from the haphazard or ignorant misuse of drugs and medicines so general a decade or more since. Some nine years ago the Council on Pharmacy and Chemistry of the American Medical Association made its first onslaught on quacks and quackery in the medicine supply business and although the Council at that time had fair reason to believe that it might be assisted in its efforts by at least the more progressive of professional pharmacists, this expected coöperation has not been forthcoming, in this country at least. Medical practitioners, largely through the American Medical Association, have been compelled to stand practically alone in their fight against the purely commercial spirit in the practice of pharmacy of to-day. The little book before us is the latest step in this warfare, representing as it does the fundamentally constructive work of the Council on Pharmacy and Chemistry, as the earlier work "Propaganda for Reform" represents the destructive work of the same body, and the now well-known book, "New and Non-official Remedies" represents a compilation of reasonably good material that is offered for future in-

clusion in the recognized materia medica of conservative medical practitioners.

The object of this, the latest of the three books offered by the Council on Pharmacy and Chemistry of the American Medical Association, is perhaps best shown by quoting rather liberally from the preface, not necessarily exactly but rather the purport of the statements made, so as to avoid occasional repetition:

"Many of the articles in the Pharmacopœia and in the National Formulary are worthless or superfluous. The repeated efforts that have been made to eliminate at least the more useless of these articles have uniformly encountered the assertion that the articles objected to are used somewhere by some one, and that they should, therefore, be officially recognized and authoritatively defined.

"For a number of years men active in the work of the Council on Medical Education and in the Confederation of State Examining and Licensing Boards have been trying to restrict instruction and examination in materia medica to the more important drugs. These efforts apparently failed, so far as the Committee of Revision of the U. S. P. is concerned, but the suggestions have been taken up and elaborated by the Council on Pharmacy and Chemistry and the result is this volume on useful drugs.

"The book is offered as a fundamental list of drugs and preparations with which all medical students and practitioners might be expected to be familiar, and to which, therefore, state examining and licensing boards might largely or entirely confine their examinations in materia medica. As it now stands, it embodies a total of about 455 headings including 265 titles of drugs and chemicals, 137 pharmaceutical preparations, 13 cross references and 40 general definitions or descriptions of forms of medicines."

It is confidently predicted that an intelligent and critical use of these selected drugs will prove their general sufficiency, and show definitely that many drugs now discussed in text books and officialized in pharmacopœias, are, to say the least, superfluous. A careful study of this book is also well designed to demonstrate that many newly discovered or widely exploited proprietary preparations have no appreciable advantage over established drugs and preparations whose limitations and possible untoward results are generally well known.

Pharmacists and teachers of pharmacy should acquaint themselves with the nature as well as the intent of the volume. The last word on a limited list of useful drugs has not as yet been said, but

the agitation will undoubtedly do much toward insuring a more uniform and better supply of recognized, standard drugs, by placing responsibility for the identity and purity of drugs and preparations on the dispensing pharmacist, where it rightly belongs. By ultimately restricting the number of drugs and preparations used it will be possible to provide adequate supervision of the medicines dispensed; and thus the pharmacist will eventually come to occupy the place he rightly deserves as an important factor in safeguarding public health. M. I. W.

WAR DEPARTMENT: Office of the Surgeon General, Bulletin No. 3. Studies of Syphilis. By Charles F. Craig, Captain, Medical Corps, U. S. Army, and Henry J. Nichols, Captain, Medical Corps, U. S. Army, with introduction by Major Frederick F. Russell, Medical Corps, U. S. Army.

This Bulletin, published for the information of medical officers by authority of the act of Congress approved August 23, 1912, and with the approval of the Secretary of War, is striking evidence of the fact that the wonderful advances made in the last decade for the diagnosis and treatment of syphilis are being made use of and appreciated by the medical men of the army. In no branch of medicine has more rapid progress been made. And, as pointed out in the introduction, "it is noteworthy that medicine is indebted to laboratory workers and research institutions, and not to the practical syphilographers, for this phenomenal progress."

Exclusive of the introduction the Bulletin consists of a series of seven papers commencing with a study of the *Spirochæta pallida*, its morphology and cultivation. Under the head of immunity the interesting statement is brought out that there is no true immunity following an infection from this parasite. A person once infected and cured can be reinfected. Opinions contrary to this were long held by the medical profession.

The diagnosis of syphilis by the complement fixation test, or Wassermann test, as it is more generally known, is gone into very fully. That this test has proven of great value in the army for diagnosis and control over treatment is attested by the experience gained from the performance of 12,000 reactions.

Ehrlich's great discovery, salvarsan and neosalvarsan, naturally, have been used and the behavior of these arsenic combinations with the benzol ring, in the treatment of syphilis is very fully gone into. The superiority of these drugs over mercury as a specific is clearly

proven; yet, in the light of our present knowledge, the consensus of opinion is that a wise combination of mercury plus salvarsan or neosalvarsan intravenously procures the best results.

The work recorded in this Bulletin clearly emphasizes the fact that the Medical Corps of the Army, in its care of our fighting men, possesses unusual facilities for the scientific observation, study, and treatment of this disease. JOHN K. THUM.

ESSENTIALS OF PRESCRIPTION WRITING. By Cary Eggleston, M.D., Instructor in Pharmacology, Cornell University Medical College, New York City. W. B. Saunders Company, Philadelphia and London.

Within the confines of this small volume which consists of only 115 pages, a medical student or graduate physician may find all the information necessary to equip himself in the principles of prescription writing, a branch of medicine in which most graduates in medicine find themselves utterly at sea when first starting practice. Some overcome this handicap and some do not; to the latter we most heartily recommend this handy little book, although, as a matter of fact, it may be read with profit by all who practise medicine.

This book consists of ten chapters which embody the fundamentals in a sequential manner; the chapter devoted to Latin grammar is brief but thorough—the author has evidently learned the art of saying much in few words—while the suggestions offered as to flavoring, coloring, and vehicles (aqueous, hydro-alcoholic and alcoholic), if carefully studied and faithfully carried out by physicians, would soon result in diminishing, if not abolishing, the proprietary medicine evil. JOHN K. THUM.

GENEALOGY OF THE DESCENDANTS OF THOMAS FRENCH, with Some Account of Colonial Manners and Doings, together with One Hundred and Fifty Picture Prints Compiled and Published by Howard Barclay French, of the Seventh Generation. Vol. II, Philadelphia. Privately printed, 1913.

Oliver Wendell Holmes once wrote that "Philadelphia was the center of genealogy." With this new contribution which is now completed, Dr. Holmes' views are confirmed. A very extended review of the first volume was given in this JOURNAL in June, 1909, p. 309. The work is handsomely gotten out and will stand as a monument to Mr. French.